REMARKS

CLAIM STATUS

Claims 1-4, and 19-26 were previously withdrawn from prosecution.

Claims 27-40 were previously cancelled.

Claim 15-18 and 43 are currently withdrawn from prosecution.

Claims 41-42 are amended herein by deleting reference to restricted sequences from these claims. No new matter is added by amendment of claims 41-42.

Claims 5-14 and 41-42 are currently pending in this application.

RESTRICTION REQUIREMENT

The Office Action sets forth a requirement for restriction as follows:

The Office Action requires that the Applicant elect one (1) polypeptide that comprises at least one mutation from claims 41-43.

THE RESTRICTION BETWEEN MARKUSH GROUP MEMBERS SHOULD BE WITHDRAWN

According to MPEP 803.02, "it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks a unity of invention. . . . Broadly, unity of invention exists where compounds included in a Markush group (1) share a common utility, and (2) share a substantial structural feature essential to that utility." Applicants note that the polypeptides that comprise at least one mutation are proper because (1) they share a common utility of "high-level expression when compared to a corresponding human factor VIII polypeptide expressed under the same conditions" and (2) they share a substantial structural feature, a conserved amino acid sequence, within 95% identity to SEQ. ID. NO.: 18 that was found surprisingly important for enhancing expression of the factor VIII molecule. See, e.g., Specification p.5, l: 26-p. 6, l:7; p. 31, l: 28-p. 32, l:18; US2005/0118684 A1 ¶ 30, 132, 133.

The Office Action restricts Markush claims 41-43 based on the assertion that "each polypeptide that comprises at least one mutation claimed is structurally and

functionally independent and distinct [because] . . . each polypeptide comprises a different mutation, each different from another." As such, the Office Action asserts that a search of more than one of the polypeptides that comprises at least one mutation claimed in claims 41-43 would require separate searches, which would be burdensome on the Office. By way of traverse to the restriction requirement alleging an improper Markush group, Applicants disagree and point out that only one search is necessary, a search of "[a]n isolated nucleic acid molecule encoding a modified factor VIII polypeptide comprising a nucleotide sequence having at least 95% sequence identity to a polynucleotide sequence shown in SEQ ID NO: 18, wherein said nucleotide sequence encodes a polypeptide characterized by high-level expression when compared to a corresponding human factor VIII polypeptide expressed under the same conditions." All possible compounds resulting from the mutations of the Markush Groups of claims 41-43 are embraced in this one search.

ELECTION

As stated previously, Applicant makes the following elections herein:

with respect to Claims 41-42, Applicant provisionally elects mutation K1245R, with traverse.

During a telephone conversation Examiner stated that an election involving claim 43 would be non-responsive due to a prior election of product claims. In the Election/Restriction Requirement mailed 8/11/2008, Examiner restricted the claims into 12 groups. Group IV contained "[C]laims 5-18, drawn to an isolated nucleic acid molecule comprising a nucleotide sequence having at least 85% sequence identity to SEQ ID NO:14, vectors, and cells comprising said nucleic acid molecule, and a method of making a polypeptide following expression of said isolated nucleic acid molecule, classifiable in class 536, subclass 23.1." In response, Applicant elected Group IV, which included process claim 15. Claim 43 is dependent upon and requires all of the limitations of claim 15. Therefore, Applicant believed that Claim 43 was properly presented.

Applicant has reviewed the Election/Restriction mailed 8/11/2008 and noted the language therein: "examiner has required restriction between product and process claims." (P.4). In consideration of the Examiner Interview and the

Examiner's apparent intent from the 8/11/2008 Restriction, Applicant has withdrawn claims 15-18 and 43 while maintaining its original traverse of the product/process restriction. Applicant makes this election only for the reason stated above and not for reasons related to patentability. Moreover, the election is made with the expectation that, when Examiner recognizes that the product claims are allowable, the requirement for restriction between the related product and process of making claims will be withdrawn, and the process claims will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 and MPEP 806.05(i). However, if Examiner allows the application to proceed with originally-elected claims 15-18 as proper members of elected Group IV, and claim 43 as properly dependent thereon, Applicant provisionally elects mutation K1245R in claim 43, with traverse of the restriction alleging an improper Markush group.

The Molecules of Claims 41-43 Share a Common Function

The Office Action asserts that the polypeptides that comprise at least one mutation are unrelated and functionally distinct because "each polypeptide comprises a different mutation, each different from another." (P. 4) This statement points out a formal difference that makes no substantive distinction meriting restriction. Accordingly, Applicant respectfully disagrees. Any permutation of mutations in the Markush groups of claims 41-43 would result in a polypeptide characterized by the same function recited in the antecedent claims:, namely, factor VIII molecules exhibiting "high level expression when compared to a corresponding human factor VIII polypeptide expressed under the same conditions." Consequently, the claims should be examined together.

The Molecules of Claims 41-43 Share a Common Structure

The Office Action asserts that the "polypeptides that comprise at least one mutation are considered to be unrelated, since each polypeptide that comprises at least one mutation claimed [in claims 41-43] is structurally and functionally independent and distinct [because] each polypeptide comprises a different mutation, each different from another." Applicants respectfully disagree.

With regard to structure, Applicant notes that any resulting polypeptides of claims 41-43 that comprise at least one mutation would comprise a polynucleotide

sequence that is between about 95.4% to 99.93% structurally identical to SEQ ID NO. 18. All of the resulting polypeptides will be factor VIII polypeptides that share an amino acid sequence (coded by a polynucleotide that shares at least 95% identity with SEQ ID NO. 18), which was found surprisingly effective for enhancing protein expression as compared to a corresponding human factor VIII polypeptide expressed under the same conditions. Consequently, they should be examined together.

For at least these reasons, claims 41-43, reciting a polypeptide further comprising at least one mutation selected from the group consisting of R503A, R508A, P511A, K1155E, T1158A, H116R, E1201D, F1203H, K1220M, K1245R, K1246N, T1249S, S1267A, and I1280V, should be examined together and the restriction between these mutations should be withdrawn.

The Subject Matter of the Search is Sufficiently Small

Applicant traverses the restriction requirement of claims 41, 42, and 43 because the subject matter of the search is sufficiently small and closely related as to be capable of examination together without presenting any undue burden. Indeed, claims 41-43, as presented, all share the limitation of "95% identity to SEQ. ID. NO.: 18." Therefore, a search of the isolated nucleic acid comprising "95% identity to SEQ. ID. NO.: 18" would necessarily encompass all of the references applicable to claims 41-43. The Markush claims merely specify possible mutations which fall within the limitation of 95% identity to SEQ. ID. NO.: 18. In fact, if all fourteen possible mutations were made in one molecule, the resulting molecules of claims 41-43 would have at least 95.4% identity to SEQ. ID. NO.: 18.

The Office Action does not specify into what class and subclass claims 41-43 belong to. However, it is clear that any permutation of mutations in the Markush groups of claims 41-43 would result in a polypeptide classifiable in class 536, subclass 23.1 - the same class in which claims 5, 6 and 15 are classified. Because the inventions have the same classification in the art (class 536, subclass 23.1): (*i*) they are of the same subject matter (polypeptides with 95% identity to SEQ. ID. NO.: 18 characterized by high level expression); and (*ii*) they require the same field of search (all will fall within class 536, subclass 23.1 and within 95% identity to SEQ.

ID. NO.: 18). Accordingly, the references applicable to one invention would necessarily be applicable to the other inventions. As a result, the search would not be an undue burden on the Office. For at least these reasons, the pending restrictions should be withdrawn and claims 41-43 should be examined as originally presented.

CONCLUSION

Applicant respectfully submits that the present application is in condition for allowance. Should Examiner feel a discussion would expedite the prosecution of this application; the Examiner is kindly invited to contact the undersigned at (312) 321-4200.

Respectfully submitted,

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